Supplementary Online Content

Khawaja AP, Rojas Lopez KE, Hardcastle AJ, et al. Genetic variants associated with corneal biomechanical properties and potentially conferring susceptibility to keratoconus in a genome-wide association study. *JAMA Ophthalmol.* Published online June 27, 2019. doi:10.1001/jamaophthalmol.2019.2058

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Participants and Analyses

EPIC-Norfolk Eye Study methods and genotyping

The European Prospective Investigation into Cancer (EPIC) study is a pan-European prospective cohort study designed to investigate the aetiology of major chronic diseases.[1] EPIC-Norfolk , one of the United Kingdom (UK) arms of EPIC, recruited and examined 25,639 participants aged 40-79 years between 1993 and 1997 for the baseline examination.[2] Recruitment was via general practices in the city of Norwich and the surrounding small towns and rural areas, and methods have been described in detail previously.[2] Since virtually all residents in the UK are registered with a general practitioner through the National Health Service, general practice lists serve as population registers. Ophthalmic assessment formed part of the third health examination and this has been termed the EPIC-Norfolk Eye Study.[3] Between 2004 and 2011 a total of 8,623 participants were seen for the ophthalmic examination. The EPIC-Norfolk Eye Study was carried out following the principles of the Declaration of Helsinki and the Research Governance Framework for Health and Social Care. The study was approved by the Norfolk Local Research Ethics Committee (05/Q0101/191) and East Norfolk & Waveney NHS Research Governance Committee (2005EC07L). All participants gave written, informed consent.

Genotyping was undertaken using the Affymetrix UK Biobank Axiom Array. SNP exclusion criteria included: call rate < 95%, abnormal cluster pattern on visual inspection, plate batch effect evident by significant variation in minor allele frequency (MAF), and/or Hardy-Weinberg equilibrium $P < 10^{-7}$. Sample exclusion criteria included: DishQC < 0.82 (poor fluorescence signal contrast), sex discordance, sample call rate < 97%, heterozygosity outliers (calculated separately for SNPs with minor allele frequency >1% and <1%), rare allele count outlier, and impossible identity-by-descent values. Following these exclusions, there were no ethnic outliers as ascertained by examining the first 5 principal components plotted against each other. Data were pre-phased using SHAPEIT version 2[4] and imputed to the Phase 3 build of the 1000 Genomes project (October 2014)[5] using IMPUTE version 2.3.2.[6]

TwinsUK methods, genotyping and sequencing

The TwinsUK is an Adult Twin Registry based at St Thomas' Hospital, London. Participants were unaware of any hypotheses or proposals for specific studies; only later were they invited to have an eye examination. The St Thomas' Hospital Local Research Ethics Committee approved the study, and all the twin participants volunteered to join the TwinsUK Registry and gave informed consent to attend

the hospital for phenotyping and for their data to be used for scientific research. The study planned to exclude subjects who had corneal refractive surgery, but no participants reported having had this done.

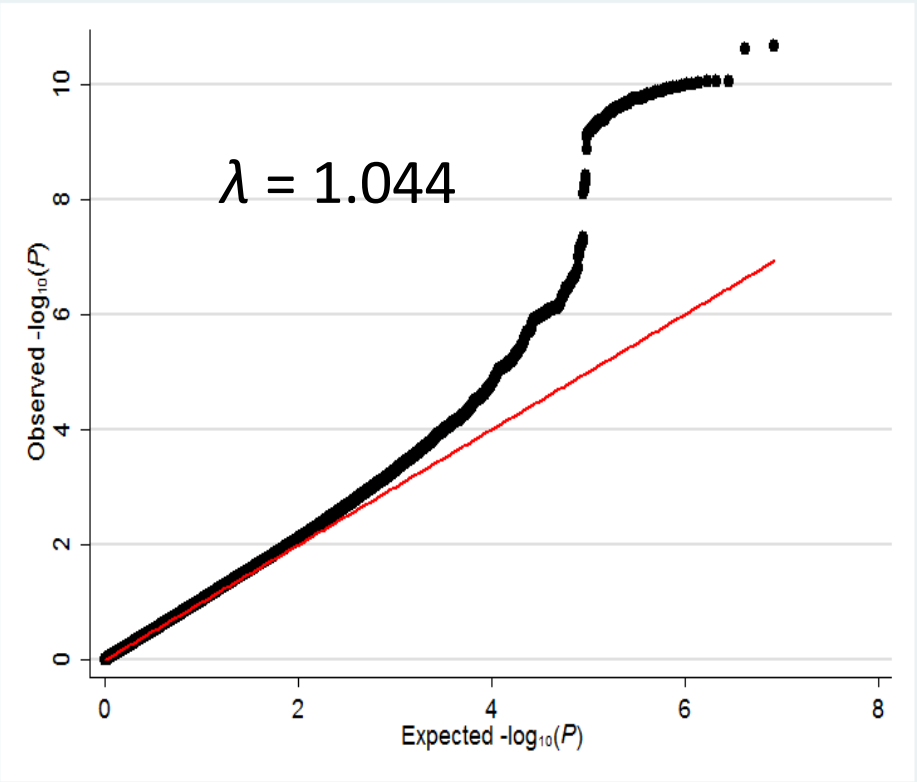
Genotyping was done using the Illumina's HumanHap610-Quad array. Genotype calling was done using the GenomeStudio Software. SNPs were removed from subsequent analyses if they had low genotyping success rate (<95%), were in Hardy-Weinberg Disequilibrium ($p<10^{-6}$), MAF different by more than 0.05 from those reported in the 1000 Genomes Project and quality control criteria for inclusion of subjects were sufficient genotyping success rate across all loci (>95%), heterozygosity within 3 standard deviations (SD) of European samples participating in the Hapmap phase 2 Project, calculated using the same exact set of SNPs that overlap between the HumanHap610-Quad array and the Hapmap phase 2 dataset. The genotypes were phased using the ShapeIt software and ungenotyped loci were imputed using IMPUTE 2.0, based on information available from the Phase 3 build of the 1000 genomes project.

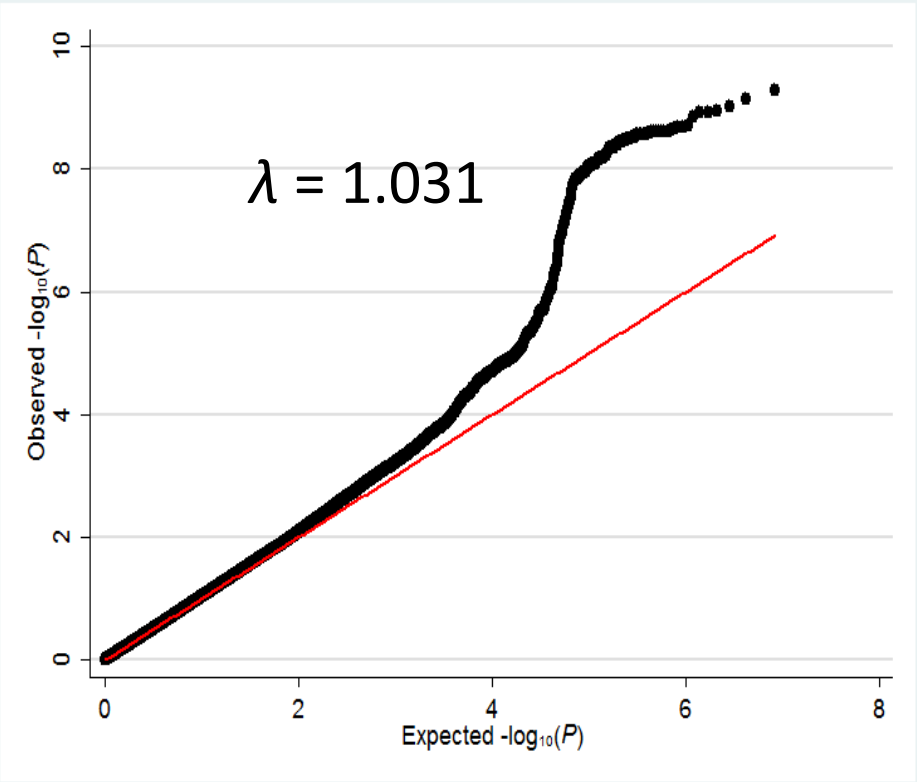
An independent subset of TwinsUK participants that did not contribute to the CH and CRF GWAS were used as controls for comparison with keratoconus cases. Whole genome sequencing was carried out in these participants as part of the UK10K project.[7] TwinsUK DNA samples, sequencing libraries and clustering were prepared following established protocols.[7] Only twins with non-admixed homogenous European ancestry as ascertained by principal component analysis of their genotypes were retained for data analysis described in this work. DNA samples were sequenced on an Illumina HiSeqX sequencer using a 150-base paired-end single-index-read format as described elsewhere.[8] Reads were mapped to human reference sequence build hg38 and variants were called using ISIS Analysis Software (v. 2.5.26.13; Illumina). Sequencing data with more than 30× coverage was obtained for a total of 2,377 whole genomes, including for 324 parents of the twins. Family relationships, including twinship and parent–offspring relations were calculated and checked for inconsistencies with self-reported relatedness. The quality metrics and filters applied to the sequencing data have been described in detail.[7] Overall, 1,960 subjects, including 383 monozygotic twins and 522 dizygotic twins, passed the quality control filtering described above, of which only subjects for whom no CRF or CH data available were compared to keratoconus patients in the case-control analysis.

Corneal tissue gene expression analysis

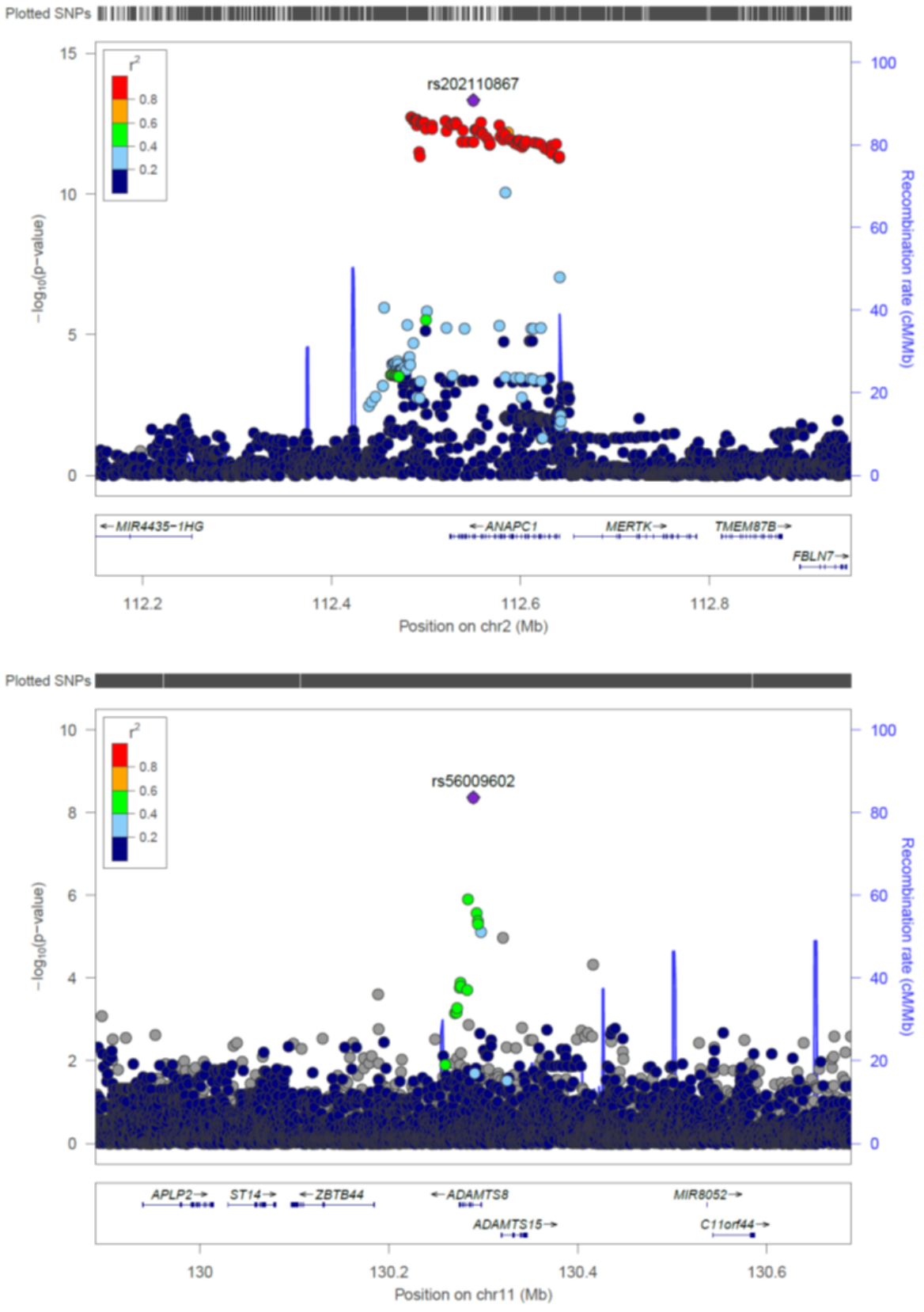
We examined the relative expression in human cornea of the genes at loci we identified as associated with CH, CRF or keratoconus. RNA-seq data from human fetal and adult corneal endothelial cells[9] and from four distinct human limbal compartments (the basal limbal crypts, the superficial limbal crypts, the paracentral/central corneal epithelium and the adjacent limbal stroma[10]) were aligned to the human genome reference hg19 and hq38 respectively using Bowtie alignment tool.[11] Gene read counts were generated using the featureCounts tool[12] and used to generate transcripts per million (TPM) values as per the formula provided by Wagner, Kin, & Lynch.[13]

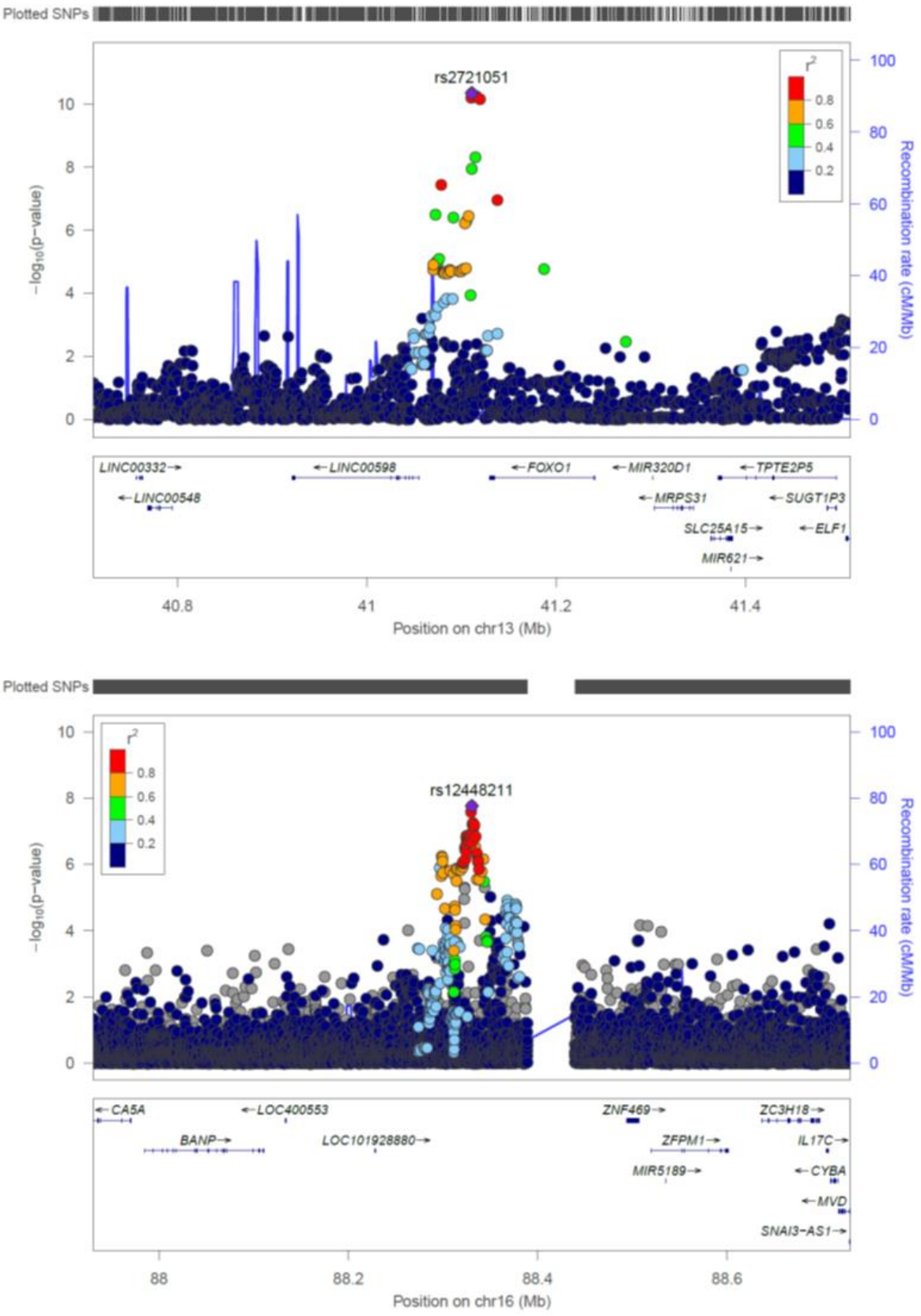
eFigure 1. Q-Q Plots for the CH (Left) and CRF (Right) Discovery GWAS in EPIC-Norfolk

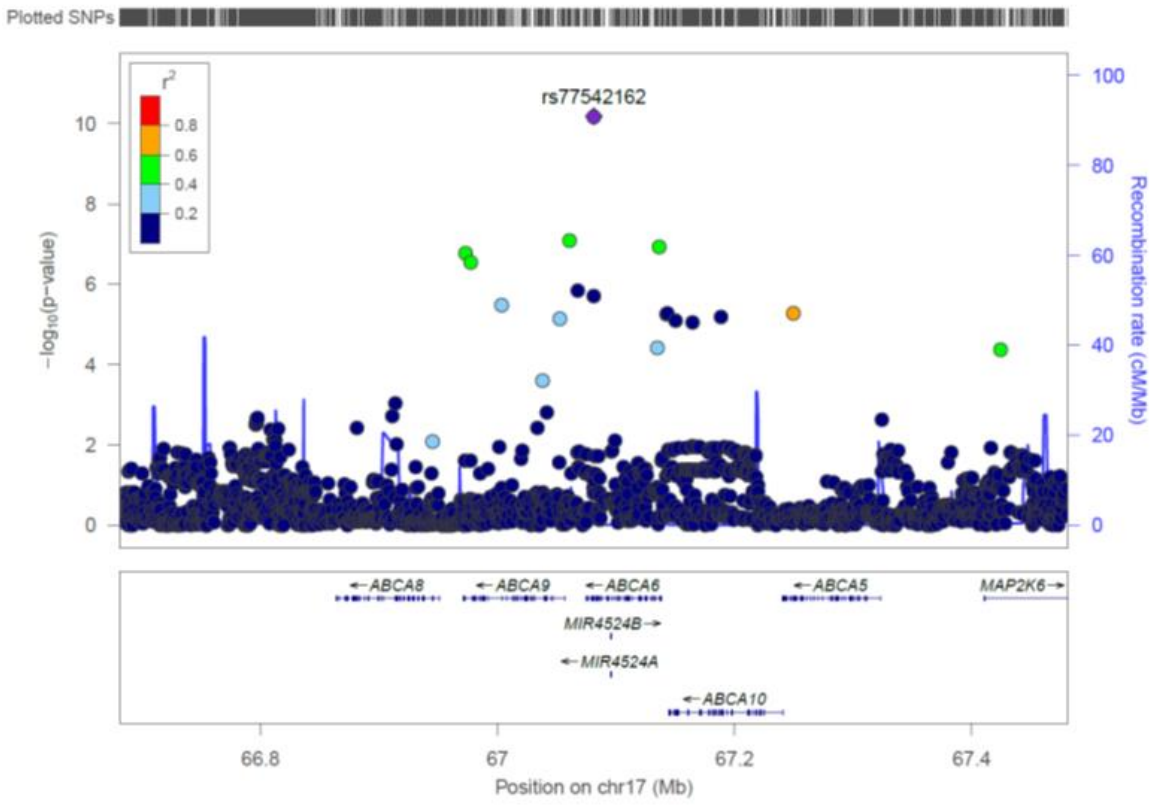




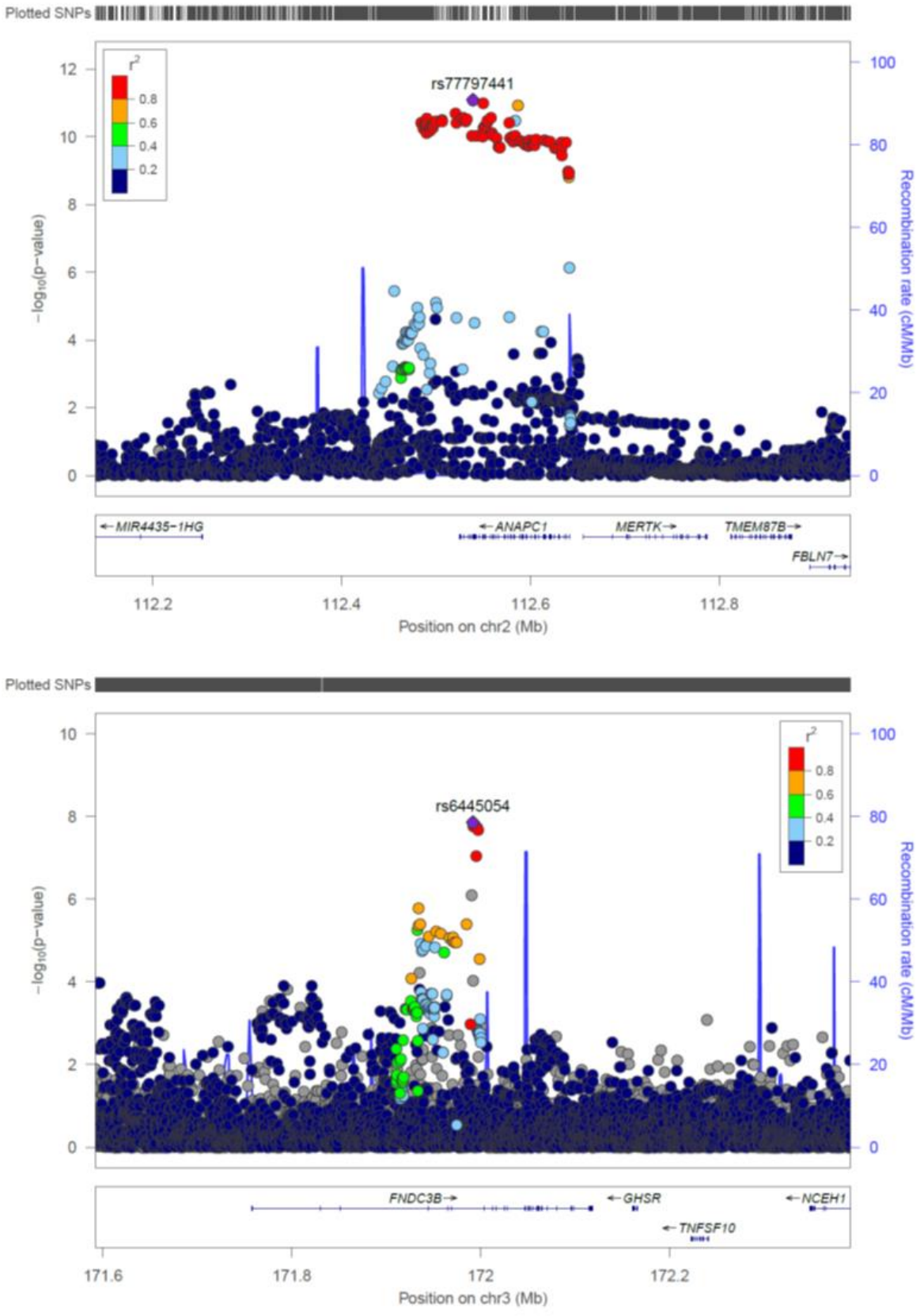
eFigure 2. LocusZoom Plots for Significant Loci From the GWAS Meta-analysis of Corneal Hysteresis in EPIC-Norfolk and TwinsUK

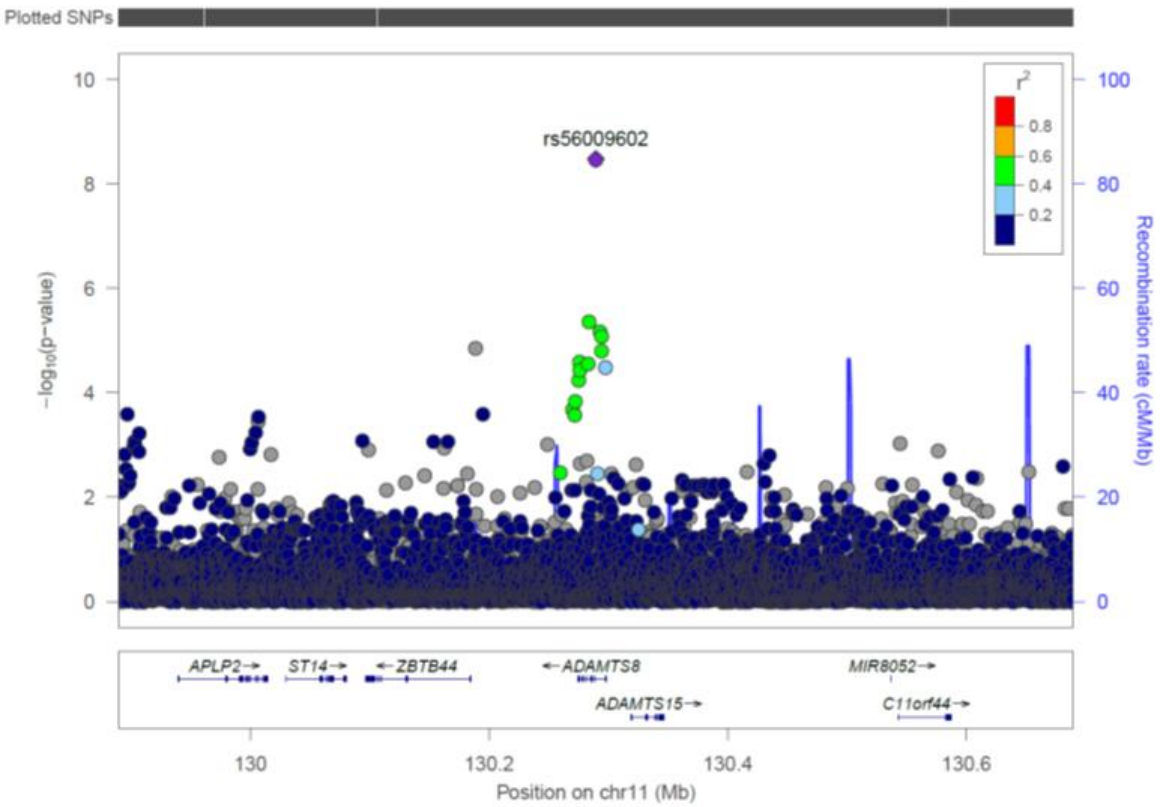


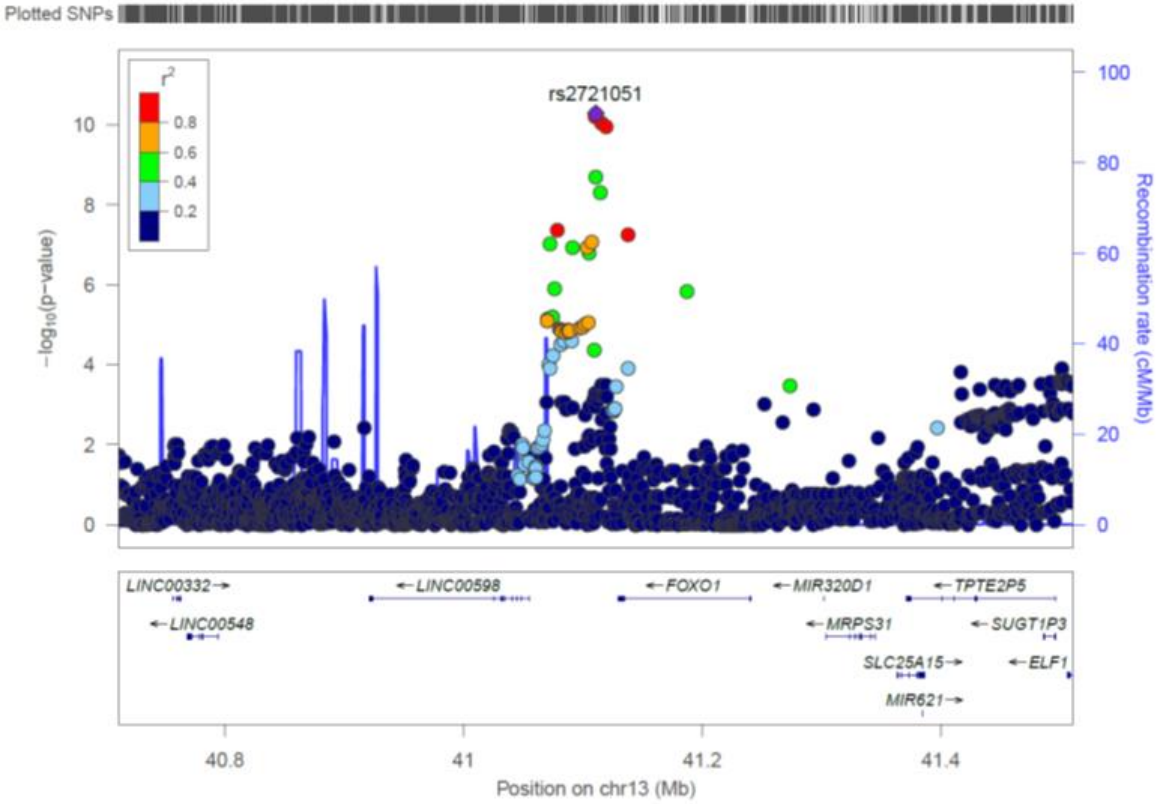


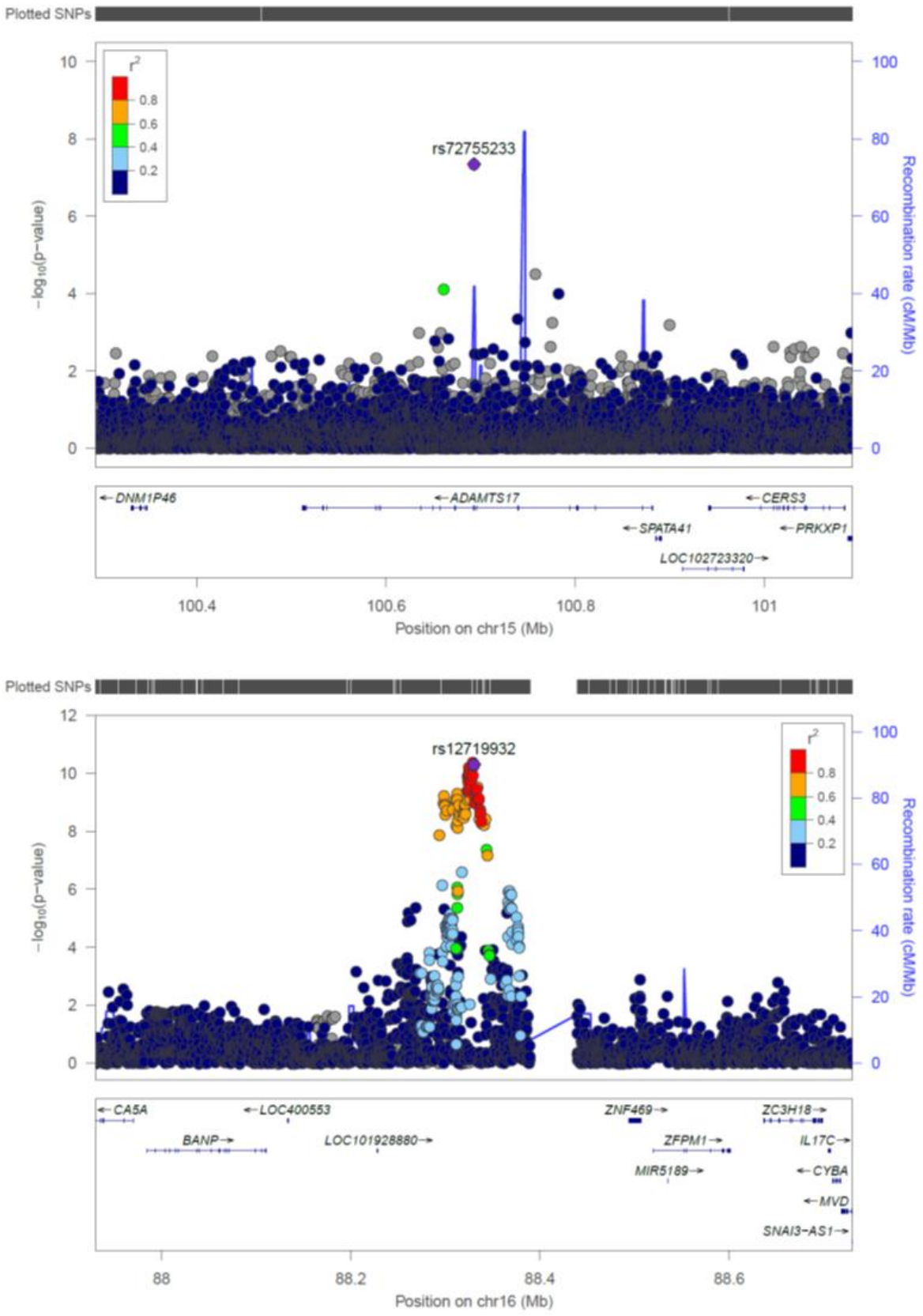


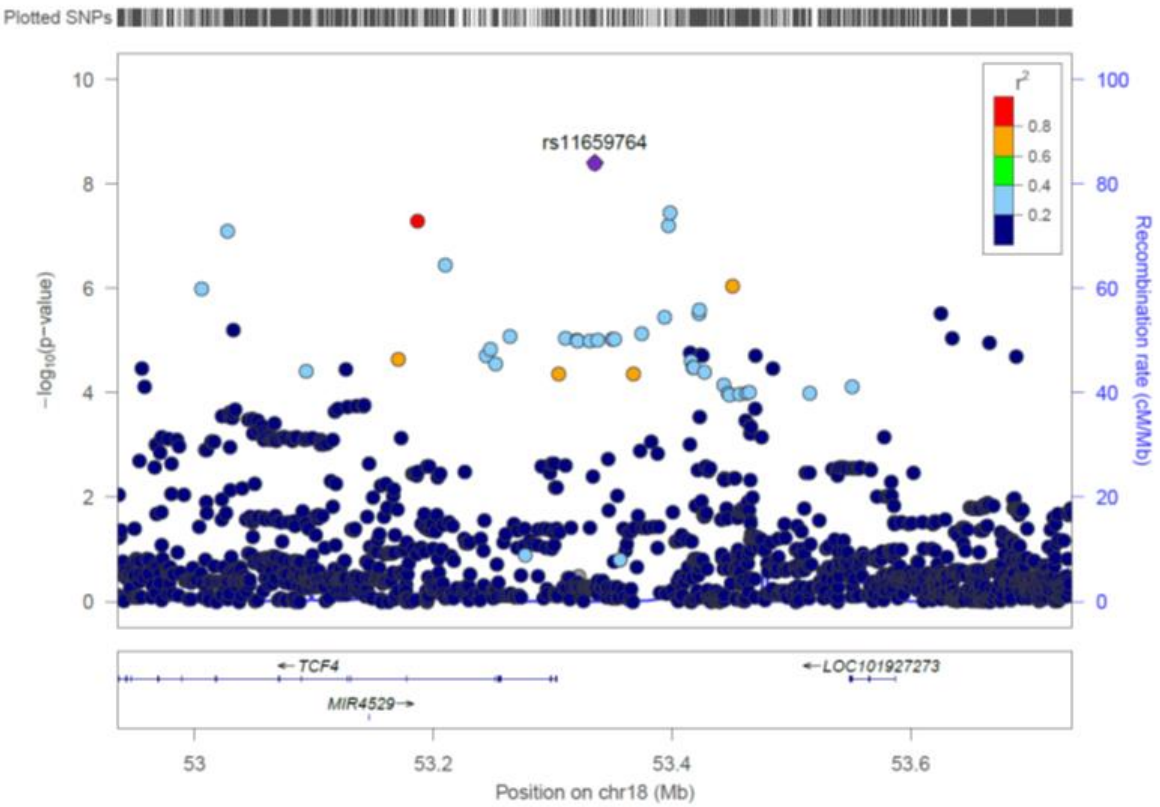
eFigure 3. LocusZoom Plots for Significant Loci From the GWAS Meta-analysis of Corneal Resistance Factor in EPIC-Norfolk and TwinsUK

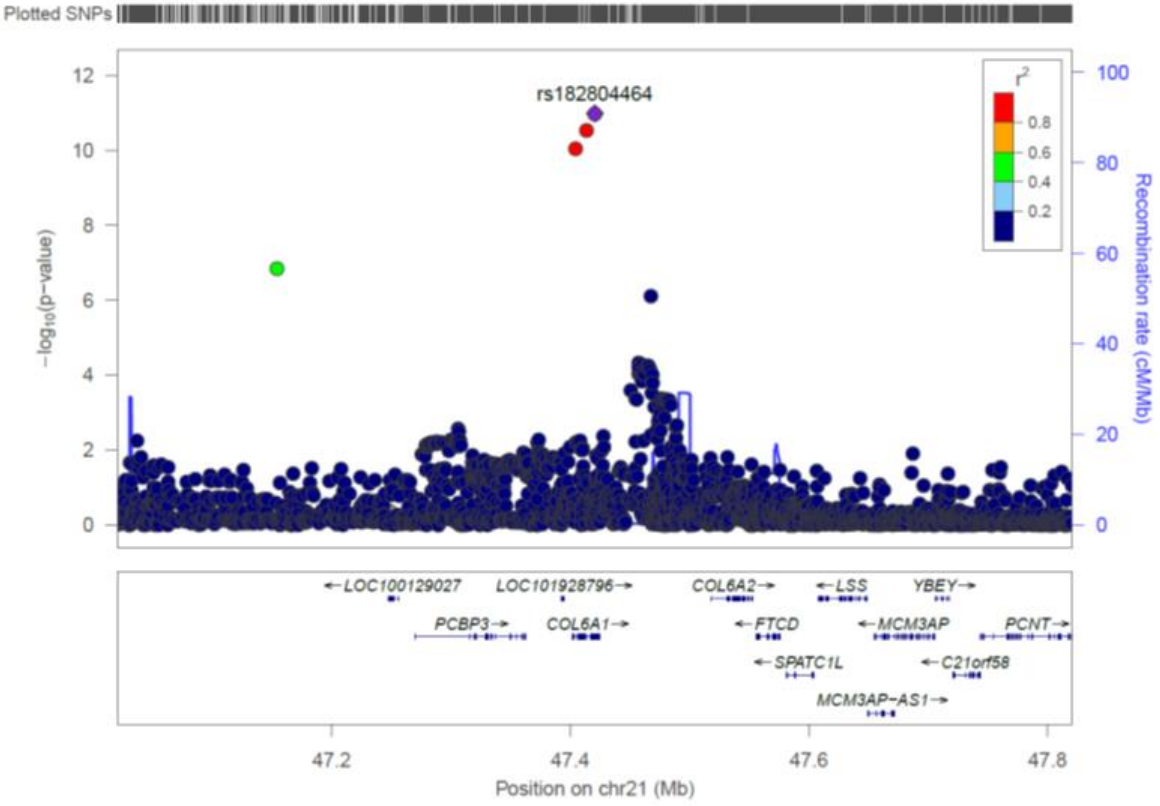






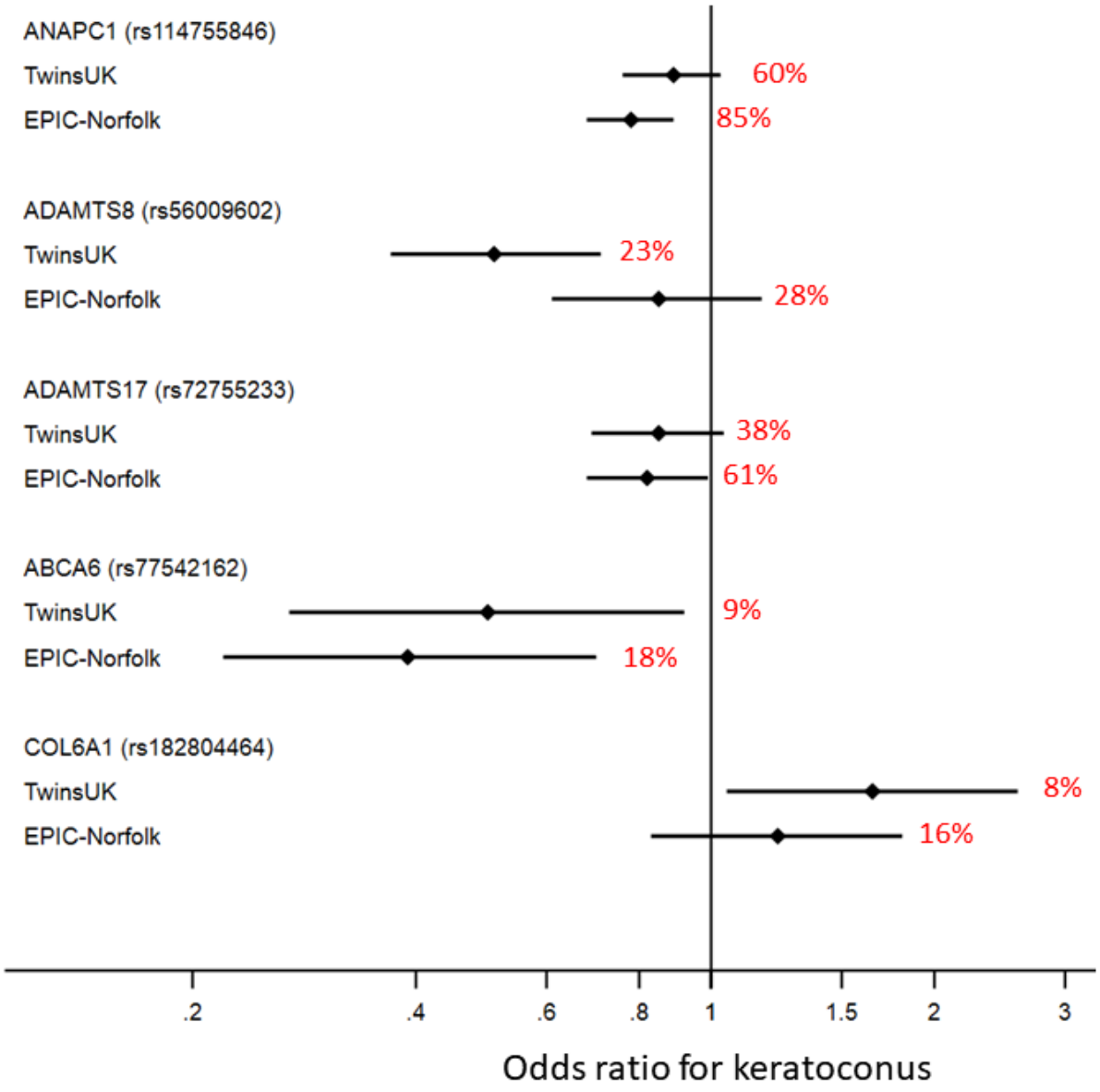






eFigure 4. Associations of Loci With Keratoconus

Results are for 752 keratoconus patients compared with either sequenced TwinsUK controls (n=974) or genotyped/imputed EPIC-Norfolk controls (n=13,828). The odds ratio and 95% confidence interval are plotted for each association. The power for detecting an odds ratio of 1.2 per effect allele with α = 0.05 is shown in red, adjacent to each effect estimate.



eTable 1. Genome-wide Significant SNPs From Corneal Hysteresis GWAS in EPIC-Norfolk

Alternate shading is used to highlight different loci, and the nearest gene at each locus is presented.

rs ID	Chr	Position	Nearest gene to locus	Effect Allele	Other Allele	Frequency of Effect Allele	Hardy-Weinberg equilibrium *P*-value	Imputation info score	Beta	Standard error	*P*-value
rs202110867	2	112550325	*ANAPC1*	G	C	0.236	0.455	0.982	0.209	0.031	2.25E-11
rs78658973	2	112484525	*ANAPC1*	A	T	0.232	0.630	0.957	0.206	0.032	8.97E-11
2:112520793	2	112520793	*ANAPC1*	G	A	0.235	0.759	0.994	0.201	0.031	8.98E-11
rs142498660	2	112484861	*ANAPC1*	T	C	0.232	0.654	0.957	0.206	0.032	9.03E-11
rs114755846	2	112520920	*ANAPC1*	T	A	0.235	0.838	0.996	0.201	0.031	9.52E-11
rs114204453	2	112486894	*ANAPC1*	A	G	0.232	0.629	0.959	0.206	0.032	1.01E-10
rs12612620	2	112488876	*ANAPC1*	A	G	0.231	0.654	0.962	0.205	0.032	1.04E-10
rs371809230	2	112489416	*ANAPC1*	A	G	0.231	0.654	0.962	0.205	0.032	1.08E-10
rs201205018	2	112490128	*ANAPC1*	A	G	0.231	0.629	0.964	0.205	0.032	1.15E-10
rs72823440	2	112490418	*ANAPC1*	A	G	0.231	0.654	0.964	0.205	0.032	1.16E-10
rs77403931	2	112490371	*ANAPC1*	G	C	0.229	0.677	0.962	0.205	0.032	1.22E-10
rs201175214	2	112559582	*ANAPC1*	G	A	0.242	0.593	0.996	0.198	0.031	1.24E-10
rs200015423	2	112558479	*ANAPC1*	G	A	0.231	0.730	0.995	0.201	0.031	1.28E-10
rs199891994	2	112495314	*ANAPC1*	D	I	0.228	0.577	0.976	0.204	0.032	1.35E-10
rs77797441	2	112539384	*ANAPC1*	T	C	0.223	0.859	0.973	0.205	0.032	1.35E-10
rs142711068	2	112560090	*ANAPC1*	A	G	0.242	0.570	0.996	0.197	0.031	1.42E-10
rs77856773	2	112493835	*ANAPC1*	D	I	0.231	0.629	0.971	0.203	0.032	1.47E-10
rs12992603	2	112598534	*ANAPC1*	G	C	0.245	0.551	0.992	0.197	0.031	1.52E-10
rs145274367	2	112494600	*ANAPC1*	A	C	0.231	0.628	0.973	0.202	0.032	1.54E-10
rs187091502	2	112577962	*ANAPC1*	T	C	0.228	0.780	0.980	0.202	0.032	1.57E-10
rs149542794	2	112496121	*ANAPC1*	A	T	0.231	0.628	0.978	0.202	0.032	1.68E-10
rs76210128	2	112532987	*ANAPC1*	T	C	0.231	0.704	0.998	0.199	0.031	1.71E-10

rs79671094	2	112531691	*ANAPC1*	A	G	0.227	0.726	0.986	0.202	0.032	1.73E-10
rs137999262	2	112526866	*ANAPC1*	A	G	0.230	0.533	1.000	0.199	0.031	1.81E-10
rs202074374	2	112564426	*ANAPC1*	C	A	0.243	0.689	0.995	0.196	0.031	1.81E-10
rs200632716	2	112496958	*ANAPC1*	A	C	0.231	0.628	0.981	0.201	0.031	1.84E-10
rs71226248	2	112506511	*ANAPC1*	T	C	0.231	0.653	0.999	0.199	0.031	1.85E-10
rs74267315	2	112498114	*ANAPC1*	G	A	0.230	0.678	0.981	0.201	0.031	1.85E-10
rs147346361	2	112529050	*ANAPC1*	G	A	0.231	0.704	0.998	0.199	0.031	1.87E-10
rs66739581	2	112580971	*ANAPC1*	C	T	0.250	0.743	1.000	0.193	0.030	1.97E-10
rs141660957	2	112554577	*ANAPC1*	T	C	0.232	0.704	0.994	0.198	0.031	2.17E-10
rs72823439	2	112490328	*ANAPC1*	G	T	0.232	0.630	0.957	0.202	0.032	2.18E-10
rs190739040	2	112552427	*ANAPC1*	T	C	0.230	0.653	0.994	0.199	0.031	2.22E-10
rs200623464	2	112554527	*ANAPC1*	T	G	0.231	0.730	0.994	0.198	0.031	2.27E-10
rs199566275	2	112513759	*ANAPC1*	D	I	0.309	0.752	0.814	0.199	0.031	2.31E-10
2:112562511	2	112562511	*ANAPC1*	D	I	0.226	1.000	0.990	0.200	0.031	2.33E-10
rs201128688	2	112566517	*ANAPC1*	T	C	0.243	0.689	0.995	0.195	0.031	2.34E-10
rs17040773	2	112500035	*ANAPC1*	C	A	0.231	0.730	1.000	0.197	0.031	2.41E-10
rs60136848	2	112582766	*ANAPC1*	D	I	0.243	0.689	0.997	0.194	0.031	2.53E-10
rs17835589	2	112641149	*ANAPC1*	C	G	0.263	0.728	0.981	0.190	0.030	2.55E-10
rs150306256	2	112506733	*ANAPC1*	C	T	0.231	0.653	0.998	0.197	0.031	2.57E-10
rs200237198	2	112543419	*ANAPC1*	I	D	0.231	0.782	0.994	0.198	0.031	2.60E-10
rs201248064	2	112503166	*ANAPC1*	D	I	0.231	0.604	0.999	0.197	0.031	2.63E-10
rs80125903	2	112549693	*ANAPC1*	A	C	0.246	0.551	0.991	0.194	0.031	2.68E-10
rs200193771	2	112538247	*ANAPC1*	A	G	0.245	0.529	0.993	0.194	0.031	2.75E-10
rs2948006	2	112521945	*ANAPC1*	A	G	0.231	0.678	0.996	0.197	0.031	2.76E-10
rs78676279	2	112543377	*ANAPC1*	T	C	0.247	0.488	0.989	0.194	0.031	2.90E-10
rs201578686	2	112567884	*ANAPC1*	I	D	0.230	0.890	0.993	0.197	0.031	3.06E-10
rs192541479	2	112552967	*ANAPC1*	T	A	0.230	0.729	0.992	0.197	0.031	3.10E-10
rs11122983	2	112584291	*ANAPC1*	A	G	0.232	0.810	0.996	0.196	0.031	3.10E-10

rs113870763	2	112567980	*ANAPC1*	C	T	0.243	0.641	0.995	0.193	0.031	3.19E-10
rs201709611	2	112567624	*ANAPC1*	G	C	0.243	0.641	0.995	0.193	0.031	3.28E-10
rs145628895	2	112503212	*ANAPC1*	D	I	0.229	0.627	0.992	0.197	0.031	3.32E-10
rs1548189	2	112633562	*ANAPC1*	T	G	0.244	0.714	0.993	0.193	0.031	3.58E-10
rs201745139	2	112578794	*ANAPC1*	C	T	0.232	0.836	0.997	0.195	0.031	3.85E-10
rs12614297	2	112583476	*ANAPC1*	T	C	0.232	0.836	0.997	0.195	0.031	3.93E-10
rs11122990	2	112599436	*ANAPC1*	T	C	0.232	0.783	0.994	0.195	0.031	4.09E-10
rs74189873	2	112606330	*ANAPC1*	A	G	0.232	0.783	0.995	0.195	0.031	4.15E-10
rs3877249	2	112615253	*ANAPC1*	T	C	0.232	0.809	0.993	0.195	0.031	4.27E-10
rs13000524	2	112637867	*ANAPC1*	G	T	0.233	0.837	0.990	0.195	0.031	4.30E-10
rs76292584	2	112619067	*ANAPC1*	A	G	0.232	0.783	0.994	0.195	0.031	4.35E-10
rs11675449	2	112589080	*ANAPC1*	A	G	0.232	0.810	0.996	0.194	0.031	4.38E-10
rs11689168	2	112621199	*ANAPC1*	C	T	0.232	0.783	0.994	0.194	0.031	4.47E-10
rs80233695	2	112633047	*ANAPC1*	C	T	0.232	0.810	0.993	0.195	0.031	4.51E-10
rs72465872	2	112631396	*ANAPC1*	D	I	0.232	0.783	0.993	0.194	0.031	4.53E-10
rs11674974	2	112591840	*ANAPC1*	G	A	0.232	0.810	0.996	0.194	0.031	4.54E-10
rs150954153	2	112581910	*ANAPC1*	G	A	0.232	0.809	0.996	0.194	0.031	4.79E-10
rs71414609	2	112640229	*ANAPC1*	A	G	0.251	0.535	0.980	0.189	0.030	4.79E-10
rs11683345	2	112597057	*ANAPC1*	T	C	0.232	0.810	0.996	0.194	0.031	4.94E-10
rs71414610	2	112641266	*ANAPC1*	C	G	0.251	0.514	0.979	0.189	0.030	4.98E-10
rs10779879	2	112603408	*ANAPC1*	T	C	0.232	0.810	0.996	0.194	0.031	5.22E-10
rs202059764	2	112578488	*ANAPC1*	D	I	0.230	0.835	0.990	0.195	0.031	5.32E-10
rs35533505	2	112640543	*ANAPC1*	C	G	0.251	0.557	0.980	0.189	0.030	5.57E-10
rs35212506	2	112594570	*ANAPC1*	G	C	0.232	0.783	0.996	0.193	0.031	5.64E-10
rs71385842	2	112628534	*ANAPC1*	D	I	0.232	0.810	0.994	0.193	0.031	5.83E-10
rs74182847	2	112604183	*ANAPC1*	G	A	0.232	0.810	0.995	0.193	0.031	5.93E-10
rs71252597	2	112492986	*ANAPC1*	C	T	0.210	0.912	0.925	0.207	0.033	5.95E-10
rs71413401	2	112604685	*ANAPC1*	C	T	0.232	0.809	0.996	0.193	0.031	6.04E-10

rs12617909	2	112598119	*ANAPC1*	T	C	0.233	0.918	0.995	0.192	0.031	6.22E-10
rs113894504	2	112633092	*ANAPC1*	G	C	0.232	0.783	0.993	0.193	0.031	6.67E-10
rs34432308	2	112626193	*ANAPC1*	T	C	0.232	0.783	0.994	0.193	0.031	6.78E-10
rs35366113	2	112629488	*ANAPC1*	A	T	0.232	0.757	0.994	0.193	0.031	6.81E-10
rs189319935	2	112550621	*ANAPC1*	G	A	0.216	0.612	0.959	0.200	0.032	6.81E-10
rs138238351	2	112610564	*ANAPC1*	D	I	0.231	0.863	0.992	0.193	0.031	6.98E-10
rs11674795	2	112602249	*ANAPC1*	T	A	0.232	0.757	0.995	0.192	0.031	6.98E-10
rs7580454	2	112587099	*ANAPC1*	T	C	0.309	0.262	0.968	0.179	0.029	7.61E-10
rs143231698	2	112493732	*ANAPC1*	G	A	0.211	0.941	0.926	0.205	0.033	8.73E-10
rs201695274	2	112617985	*ANAPC1*	I	D	0.207	0.765	0.923	0.204	0.034	1.41E-09
rs34739497	2	112625267	*ANAPC1*	D	I	0.320	0.398	0.917	0.171	0.029	7.07E-09
rs56307072	2	112584242	*ANAPC1*	T	A	0.329	0.420	0.841	0.169	0.031	3.09E-08
rs2721051	13	41110884	*FOXO1*	T	C	0.108	0.751	1.000	-0.248	0.042	4.06E-09
rs148496467	13	41112152	*FOXO1*	I	D	0.108	0.751	0.999	-0.247	0.042	4.48E-09
rs2755238	13	41110270	*FOXO1*	C	T	0.108	0.849	0.998	-0.246	0.042	5.38E-09
rs2701857	13	41115586	*FOXO1*	C	A	0.108	0.750	0.996	-0.246	0.042	5.66E-09
rs11616662	13	41119466	*FOXO1*	A	G	0.108	0.751	0.990	-0.244	0.042	7.93E-09
rs79728429	13	41114572	*FOXO1*	T	C	0.065	0.267	1.000	-0.288	0.053	4.61E-08
rs77542162	17	67081278	*ABCA6*	G	A	0.021	1.000	1.000	0.613	0.092	2.55E-11

eTable 2. Genome-wide Significant SNPs From Corneal Resistance Factor GWAS in EPIC-Norfolk

Alternate shading is used to highlight different loci, and the nearest gene at each locus is presented.

rs ID	Chr	Position	Nearest gene at locus	Effect Allele	Other Allele	Frequency of Effect Allele	Hardy-Weinberg equilibrium *P*-value	Imputation info score	Beta	Standard error	*P*-value
rs77797441	2	112539384	*ANAPC1*	T	C	0.223	0.859	0.973	0.218	0.035	5.11E-10
rs202110867	2	112550325	*ANAPC1*	G	C	0.236	0.455	0.982	0.212	0.034	7.14E-10
2:112520793	2	112520793	*ANAPC1*	G	A	0.235	0.759	0.994	0.206	0.034	1.42E-09
rs114755846	2	112520920	*ANAPC1*	T	A	0.235	0.838	0.996	0.205	0.034	1.92E-09
rs200015423	2	112558479	*ANAPC1*	G	A	0.231	0.730	0.995	0.206	0.034	2.08E-09
rs77403931	2	112490371	*ANAPC1*	G	C	0.229	0.677	0.962	0.210	0.035	2.15E-09
rs147346361	2	112529050	*ANAPC1*	G	A	0.231	0.704	0.998	0.205	0.034	2.38E-09
rs17040773	2	112500035	*ANAPC1*	C	A	0.231	0.730	1.000	0.204	0.034	2.40E-09
rs78658973	2	112484525	*ANAPC1*	A	T	0.232	0.630	0.957	0.209	0.035	2.43E-09
rs71226248	2	112506511	*ANAPC1*	T	C	0.231	0.653	0.999	0.205	0.034	2.43E-09
rs76210128	2	112532987	*ANAPC1*	T	C	0.231	0.704	0.998	0.204	0.034	2.49E-09
rs137999262	2	112526866	*ANAPC1*	A	G	0.230	0.533	1.000	0.205	0.034	2.49E-09
rs12612620	2	112488876	*ANAPC1*	A	G	0.231	0.654	0.962	0.208	0.035	2.50E-09
rs142498660	2	112484861	*ANAPC1*	T	C	0.232	0.654	0.957	0.208	0.035	2.52E-09
rs371809230	2	112489416	*ANAPC1*	A	G	0.231	0.654	0.962	0.208	0.035	2.59E-09
rs141660957	2	112554577	*ANAPC1*	T	C	0.232	0.704	0.994	0.204	0.034	2.69E-09
rs145628895	2	112503212	*ANAPC1*	D	I	0.229	0.627	0.992	0.205	0.034	2.72E-09
rs150306256	2	112506733	*ANAPC1*	C	T	0.231	0.653	0.998	0.204	0.034	2.75E-09
rs72823440	2	112490418	*ANAPC1*	A	G	0.231	0.654	0.964	0.207	0.035	2.76E-09
rs201248064	2	112503166	*ANAPC1*	D	I	0.231	0.604	0.999	0.204	0.034	2.77E-09
rs71252597	2	112492986	*ANAPC1*	C	T	0.210	0.912	0.925	0.218	0.037	2.79E-09
rs56307072	2	112584242	*ANAPC1*	T	A	0.329	0.420	0.841	0.200	0.034	2.87E-09

rs74267315	2	112498114	*ANAPC1*	G	A	0.230	0.678	0.981	0.205	0.035	3.04E-09
rs2948006	2	112521945	*ANAPC1*	A	G	0.231	0.678	0.996	0.204	0.034	3.04E-09
rs200623464	2	112554527	*ANAPC1*	T	G	0.231	0.730	0.994	0.203	0.034	3.07E-09
rs187091502	2	112577962	*ANAPC1*	T	C	0.228	0.780	0.980	0.206	0.035	3.16E-09
rs199891994	2	112495314	*ANAPC1*	D	I	0.228	0.577	0.976	0.206	0.035	3.23E-09
rs200237198	2	112543419	*ANAPC1*	I	D	0.231	0.782	0.994	0.203	0.034	3.31E-09
rs143231698	2	112493732	*ANAPC1*	G	A	0.211	0.941	0.926	0.217	0.037	3.34E-09
rs190739040	2	112552427	*ANAPC1*	T	C	0.230	0.653	0.994	0.203	0.034	3.44E-09
rs114204453	2	112486894	*ANAPC1*	A	G	0.232	0.629	0.959	0.207	0.035	3.46E-09
rs201205018	2	112490128	*ANAPC1*	A	G	0.231	0.629	0.964	0.206	0.035	3.51E-09
rs145274367	2	112494600	*ANAPC1*	A	C	0.231	0.628	0.973	0.205	0.035	3.66E-09
rs79671094	2	112531691	*ANAPC1*	A	G	0.227	0.726	0.986	0.205	0.035	3.67E-09
rs149542794	2	112496121	*ANAPC1*	A	T	0.231	0.628	0.978	0.204	0.035	4.08E-09
rs200632716	2	112496958	*ANAPC1*	A	C	0.231	0.628	0.981	0.203	0.035	4.39E-09
rs77856773	2	112493835	*ANAPC1*	D	I	0.231	0.629	0.971	0.204	0.035	4.46E-09
rs192541479	2	112552967	*ANAPC1*	T	A	0.230	0.729	0.992	0.202	0.034	4.52E-09
rs201175214	2	112559582	*ANAPC1*	G	A	0.242	0.593	0.996	0.198	0.034	4.69E-09
2:112562511	2	112562511	*ANAPC1*	D	I	0.226	1.000	0.990	0.202	0.035	5.42E-09
rs200193771	2	112538247	*ANAPC1*	A	G	0.245	0.529	0.993	0.196	0.034	5.77E-09
rs142711068	2	112560090	*ANAPC1*	A	G	0.242	0.570	0.996	0.197	0.034	5.78E-09
rs80125903	2	112549693	*ANAPC1*	A	C	0.246	0.551	0.991	0.196	0.034	6.01E-09
rs78676279	2	112543377	*ANAPC1*	T	C	0.247	0.488	0.989	0.196	0.034	6.32E-09
rs72823439	2	112490328	*ANAPC1*	G	T	0.232	0.630	0.957	0.203	0.035	6.38E-09
rs202074374	2	112564426	*ANAPC1*	C	A	0.243	0.689	0.995	0.196	0.034	6.67E-09
rs11122983	2	112584291	*ANAPC1*	A	G	0.232	0.810	0.996	0.198	0.034	7.05E-09
rs189319935	2	112550621	*ANAPC1*	G	A	0.216	0.612	0.959	0.206	0.036	7.84E-09
rs13000524	2	112637867	*ANAPC1*	G	T	0.233	0.837	0.990	0.198	0.034	8.10E-09
rs3877249	2	112615253	*ANAPC1*	T	C	0.232	0.809	0.993	0.198	0.034	8.14E-09

rs74189873	2	112606330	*ANAPC1*	A	G	0.232	0.783	0.995	0.197	0.034	8.29E-09
rs80233695	2	112633047	*ANAPC1*	C	T	0.232	0.810	0.993	0.197	0.034	8.43E-09
rs12992603	2	112598534	*ANAPC1*	G	C	0.245	0.551	0.992	0.194	0.034	8.47E-09
rs72465872	2	112631396	*ANAPC1*	D	I	0.232	0.783	0.993	0.197	0.034	8.50E-09
rs11689168	2	112621199	*ANAPC1*	C	T	0.232	0.783	0.994	0.197	0.034	8.51E-09
rs201745139	2	112578794	*ANAPC1*	C	T	0.232	0.836	0.997	0.197	0.034	8.59E-09
rs76292584	2	112619067	*ANAPC1*	A	G	0.232	0.783	0.994	0.197	0.034	8.88E-09
rs11122990	2	112599436	*ANAPC1*	T	C	0.232	0.783	0.994	0.197	0.034	8.99E-09
rs7580454	2	112587099	*ANAPC1*	T	C	0.309	0.262	0.968	0.183	0.032	9.23E-09
rs12614297	2	112583476	*ANAPC1*	T	C	0.232	0.836	0.997	0.197	0.034	9.29E-09
rs11675449	2	112589080	*ANAPC1*	A	G	0.232	0.810	0.996	0.196	0.034	9.68E-09
rs11674974	2	112591840	*ANAPC1*	G	A	0.232	0.810	0.996	0.196	0.034	9.97E-09
rs11683345	2	112597057	*ANAPC1*	T	C	0.232	0.810	0.996	0.196	0.034	1.06E-08
rs74182847	2	112604183	*ANAPC1*	G	A	0.232	0.810	0.995	0.196	0.034	1.07E-08
rs10779879	2	112603408	*ANAPC1*	T	C	0.232	0.810	0.996	0.196	0.034	1.10E-08
rs150954153	2	112581910	*ANAPC1*	G	A	0.232	0.809	0.996	0.196	0.034	1.10E-08
rs11674795	2	112602249	*ANAPC1*	T	A	0.232	0.757	0.995	0.196	0.034	1.12E-08
rs71385842	2	112628534	*ANAPC1*	D	I	0.232	0.810	0.994	0.196	0.034	1.14E-08
rs66739581	2	112580971	*ANAPC1*	C	T	0.250	0.743	1.000	0.190	0.033	1.16E-08
rs71414609	2	112640229	*ANAPC1*	A	G	0.251	0.535	0.980	0.191	0.033	1.16E-08
rs201578686	2	112567884	*ANAPC1*	I	D	0.230	0.890	0.993	0.196	0.034	1.19E-08
rs202059764	2	112578488	*ANAPC1*	D	I	0.230	0.835	0.990	0.196	0.034	1.25E-08
rs201128688	2	112566517	*ANAPC1*	T	C	0.243	0.689	0.995	0.192	0.034	1.25E-08
rs35212506	2	112594570	*ANAPC1*	G	C	0.232	0.783	0.996	0.195	0.034	1.27E-08
rs113870763	2	112567980	*ANAPC1*	C	T	0.243	0.641	0.995	0.192	0.034	1.30E-08
rs201709611	2	112567624	*ANAPC1*	G	C	0.243	0.641	0.995	0.192	0.034	1.31E-08
rs12617909	2	112598119	*ANAPC1*	T	C	0.233	0.918	0.995	0.194	0.034	1.33E-08
rs71414610	2	112641266	*ANAPC1*	C	G	0.251	0.514	0.979	0.190	0.033	1.34E-08

rs71413401	2	112604685	*ANAPC1*	C	T	0.232	0.809	0.996	0.194	0.034	1.37E-08
rs35366113	2	112629488	*ANAPC1*	A	T	0.232	0.757	0.994	0.195	0.034	1.40E-08
rs60136848	2	112582766	*ANAPC1*	D	I	0.243	0.689	0.997	0.191	0.034	1.41E-08
rs113894504	2	112633092	*ANAPC1*	G	C	0.232	0.783	0.993	0.194	0.034	1.42E-08
rs34432308	2	112626193	*ANAPC1*	T	C	0.232	0.783	0.994	0.194	0.034	1.45E-08
rs35533505	2	112640543	*ANAPC1*	C	G	0.251	0.557	0.980	0.189	0.033	1.46E-08
rs17835589	2	112641149	*ANAPC1*	C	G	0.263	0.728	0.981	0.187	0.033	1.48E-08
rs138238351	2	112610564	*ANAPC1*	D	I	0.231	0.863	0.992	0.194	0.034	1.68E-08
rs1548189	2	112633562	*ANAPC1*	T	G	0.244	0.714	0.993	0.190	0.034	1.69E-08
rs34739497	2	112625267	*ANAPC1*	D	I	0.320	0.398	0.917	0.182	0.032	2.01E-08
rs201695274	2	112617985	*ANAPC1*	I	D	0.207	0.765	0.923	0.203	0.037	4.40E-08
rs2721051	13	41110884	*FOXO1*	T	C	0.108	0.751	1.000	-0.268	0.046	6.79E-09
rs148496467	13	41112152	*FOXO1*	I	D	0.108	0.751	0.999	-0.267	0.046	8.03E-09
rs2755238	13	41110270	*FOXO1*	C	T	0.108	0.849	0.998	-0.267	0.046	8.37E-09
rs2701857	13	41115586	*FOXO1*	C	A	0.108	0.750	0.996	-0.265	0.046	1.10E-08
rs11616662	13	41119466	*FOXO1*	A	G	0.108	0.751	0.990	-0.263	0.046	1.55E-08
rs74948688	13	41110922	*FOXO1*	T	C	0.071	0.926	0.984	-0.311	0.056	3.27E-08
rs79728429	13	41114572	*FOXO1*	T	C	0.065	0.267	1.000	-0.316	0.058	4.63E-08
rs12719932	16	88330349	*ZNF469*	G	A	0.637	0.105	0.991	0.182	0.030	9.39E-10
rs12448211	16	88330513	*ZNF469*	A	G	0.637	0.106	0.993	0.181	0.030	1.11E-09
rs28378192	16	88329660	*ZNF469*	T	C	0.636	0.124	0.990	0.181	0.030	1.18E-09
rs28687756	16	88328928	*ZNF469*	G	T	0.662	0.217	0.964	0.187	0.031	1.21E-09
rs35193497	16	88324821	*ZNF469*	G	T	0.662	0.125	0.983	0.182	0.030	2.07E-09
rs28526212	16	88329202	*ZNF469*	A	G	0.650	0.225	0.989	0.180	0.030	2.35E-09
rs28698209	16	88324931	*ZNF469*	G	T	0.661	0.132	0.980	0.180	0.030	3.50E-09
rs28411862	16	88325560	*ZNF469*	C	G	0.337	0.146	0.984	-0.179	0.030	3.82E-09
rs34715091	16	88326782	*ZNF469*	G	A	0.352	0.197	0.985	-0.177	0.030	4.01E-09
rs11259972	16	88333296	*ZNF469*	C	T	0.632	0.114	0.992	0.174	0.030	4.13E-09

rs28563118	16	88327569	*ZNF469*	G	C	0.349	0.177	0.987	-0.177	0.030	4.28E-09
rs8059298	16	88332479	*ZNF469*	C	T	0.632	0.114	0.995	0.174	0.030	4.39E-09
rs35479534	16	88324754	*ZNF469*	A	G	0.663	0.138	0.985	0.178	0.030	4.44E-09
rs28445880	16	88327422	*ZNF469*	T	G	0.347	0.129	0.988	-0.177	0.030	4.47E-09
rs28425635	16	88323599	*ZNF469*	G	A	0.340	0.140	0.985	-0.177	0.030	5.70E-09
rs9922572	16	88334112	*ZNF469*	C	A	0.666	0.440	0.968	0.179	0.031	6.56E-09
rs146769134	16	88323048	*ZNF469*	D	I	0.338	0.132	0.985	-0.176	0.030	6.64E-09
rs28493272	16	88324245	*ZNF469*	T	C	0.338	0.139	0.985	-0.176	0.030	6.73E-09
rs149051942	16	88322836	*ZNF469*	I	D	0.338	0.118	0.985	-0.176	0.030	6.93E-09
rs28716598	16	88324563	*ZNF469*	G	C	0.664	0.117	0.985	0.176	0.030	7.02E-09
rs58577366	16	88323323	*ZNF469*	C	T	0.337	0.111	0.985	-0.175	0.030	8.04E-09
rs9926214	16	88334441	*ZNF469*	T	C	0.641	0.135	0.980	0.173	0.030	8.14E-09
rs28715745	16	88324562	*ZNF469*	A	G	0.660	0.085	0.982	0.175	0.030	8.78E-09
rs12926024	16	88331309	*ZNF469*	C	T	0.634	0.139	0.997	0.170	0.030	9.49E-09
rs9934580	16	88331515	*ZNF469*	G	A	0.634	0.153	0.997	0.169	0.030	1.23E-08
rs9938149	16	88331640	*ZNF469*	A	C	0.633	0.170	1.000	0.169	0.030	1.26E-08
rs12719931	16	88335776	*ZNF469*	T	C	0.650	0.205	0.982	0.172	0.030	1.35E-08
rs12719930	16	88335774	*ZNF469*	A	G	0.650	0.205	0.982	0.171	0.030	1.47E-08
rs28481824	16	88326166	*ZNF469*	T	C	0.332	0.092	0.985	-0.172	0.030	1.69E-08
rs141625840	16	88322876	*ZNF469*	I	D	0.297	0.100	0.925	-0.182	0.032	1.98E-08
rs58664271	16	88322455	*ZNF469*	D	I	0.340	0.101	0.980	-0.170	0.030	2.25E-08
rs12919641	16	88312600	*ZNF469*	C	G	0.668	0.184	0.974	0.170	0.031	2.85E-08
rs8057716	16	88335790	*ZNF469*	C	G	0.667	0.334	0.982	0.170	0.031	2.95E-08
rs58657775	16	88323829	*ZNF469*	G	A	0.346	0.193	0.985	-0.168	0.030	3.05E-08
rs12935558	16	88336978	*ZNF469*	A	G	0.641	0.150	0.981	0.166	0.030	3.18E-08
rs12935576	16	88337013	*ZNF469*	A	G	0.641	0.150	0.982	0.166	0.030	3.52E-08
rs12918094	16	88337319	*ZNF469*	G	A	0.641	0.150	0.981	0.166	0.030	3.55E-08
rs7501109	16	88320862	*ZNF469*	C	G	0.655	0.135	0.989	0.166	0.030	4.01E-08

rs6540217	16	88310910	*ZNF469*	G	A	0.658	0.127	0.984	0.166	0.030	4.04E-08
rs7403826	16	88321167	*ZNF469*	T	A	0.656	0.150	0.988	0.165	0.030	4.85E-08
rs7404292	16	88338467	*ZNF469*	G	A	0.667	0.407	0.980	0.168	0.031	4.88E-08
rs149540885	18	52877255	*TCF4*	C	T	0.027	0.243	0.964	-0.512	0.091	1.79E-08
rs11659764	18	53335512	*TCF4*	A	T	0.056	1.000	0.990	-0.349	0.063	2.55E-08
rs182804464	21	47420667	*COL6A1*	G	C	0.016	0.678	0.978	-0.694	0.117	2.83E-09
rs142493024	21	47413793	*COL6A1*	A	G	0.016	0.680	0.968	-0.681	0.117	6.45E-09
rs148766287	21	47404422	*COL6A1*	G	C	0.016	0.684	0.959	-0.661	0.117	1.78E-08

eTable 3. Genome-wide Significant SNPs From Meta-analysis of Corneal Hysteresis GWAS in EPIC-Norfolk and TwinsUK

Alternate shading is used to highlight different loci, and the nearest gene at each locus is presented.

rs ID	Chromosome	Position	Nearest gene to locus	Allele 1	Allele 2	Beta	Standard error	*P*-value	Direction	I-squared
rs78658973	2	112484525	*ANAPC1*	a	t	0.207	0.028	1.79E-13	++	0
rs142498660	2	112484861	*ANAPC1*	t	c	0.207	0.028	1.78E-13	++	0
rs114204453	2	112486894	*ANAPC1*	a	g	0.206	0.028	2.20E-13	++	0
rs12612620	2	112488876	*ANAPC1*	a	g	0.206	0.028	2.20E-13	++	0
rs371809230	2	112489416	*ANAPC1*	a	g	0.206	0.028	2.26E-13	++	0
rs201205018	2	112490128	*ANAPC1*	a	g	0.206	0.028	2.41E-13	++	0
rs72823439	2	112490328	*ANAPC1*	t	g	-0.205	0.028	3.33E-13	--	0
rs77403931	2	112490371	*ANAPC1*	c	g	-0.206	0.028	2.07E-13	--	0
rs72823440	2	112490418	*ANAPC1*	a	g	0.206	0.028	2.39E-13	++	0
rs71252597	2	112492986	*ANAPC1*	t	c	-0.206	0.030	3.01E-12	--	0
rs143231698	2	112493732	*ANAPC1*	a	g	-0.204	0.030	4.39E-12	--	0
rs145274367	2	112494600	*ANAPC1*	a	c	0.204	0.028	2.71E-13	++	0
rs149542794	2	112496121	*ANAPC1*	a	t	0.204	0.028	2.83E-13	++	0
rs200632716	2	112496958	*ANAPC1*	a	c	0.203	0.028	3.12E-13	++	0
rs74267315	2	112498114	*ANAPC1*	a	g	-0.204	0.028	2.66E-13	--	0
rs17040773	2	112500035	*ANAPC1*	a	c	-0.199	0.027	4.68E-13	--	0
rs71226248	2	112506511	*ANAPC1*	t	c	0.200	0.027	3.41E-13	++	0
rs150306256	2	112506733	*ANAPC1*	t	c	-0.199	0.027	4.65E-13	--	0
2:112520793	2	112520793	*ANAPC1*	a	g	-0.199	0.027	2.28E-13	--	0
rs114755846	2	112520920	*ANAPC1*	a	t	-0.199	0.027	2.43E-13	--	0
rs2948006	2	112521945	*ANAPC1*	a	g	0.198	0.027	5.52E-13	++	0
rs137999262	2	112526866	*ANAPC1*	a	g	0.199	0.027	3.29E-13	++	0

rs147346361	2	112529050	*ANAPC1*	a	g	-0.199	0.027	3.24E-13	--	0
rs79671094	2	112531691	*ANAPC1*	a	g	0.203	0.028	2.65E-13	++	0
rs76210128	2	112532987	*ANAPC1*	t	c	0.199	0.027	3.20E-13	++	0
rs200193771	2	112538247	*ANAPC1*	a	g	0.190	0.027	1.36E-12	++	0
rs77797441	2	112539384	*ANAPC1*	t	c	0.203	0.028	5.06E-13	++	0
rs78676279	2	112543377	*ANAPC1*	t	c	0.191	0.027	1.35E-12	++	0
rs80125903	2	112549693	*ANAPC1*	a	c	0.191	0.027	1.36E-12	++	0
rs202110867	2	112550325	*ANAPC1*	c	g	-0.207	0.027	4.43E-14	--	0
rs189319935	2	112550621	*ANAPC1*	a	g	-0.202	0.028	1.33E-12	--	0
rs190739040	2	112552427	*ANAPC1*	t	c	0.199	0.027	4.86E-13	++	0
rs192541479	2	112552967	*ANAPC1*	a	t	-0.199	0.027	5.24E-13	--	0
rs200623464	2	112554527	*ANAPC1*	t	g	0.198	0.027	4.56E-13	++	0
rs141660957	2	112554577	*ANAPC1*	t	c	0.198	0.027	4.46E-13	++	0
rs200015423	2	112558479	*ANAPC1*	a	g	-0.200	0.027	2.70E-13	--	0
rs201175214	2	112559582	*ANAPC1*	a	g	-0.194	0.027	6.22E-13	--	0
rs142711068	2	112560090	*ANAPC1*	a	g	0.193	0.027	7.06E-13	++	0
rs202074374	2	112564426	*ANAPC1*	a	c	-0.192	0.027	9.14E-13	--	0
rs201128688	2	112566517	*ANAPC1*	t	c	0.191	0.027	1.20E-12	++	0
rs201709611	2	112567624	*ANAPC1*	c	g	-0.190	0.027	1.66E-12	--	0
rs113870763	2	112567980	*ANAPC1*	t	c	-0.190	0.027	1.62E-12	--	0
rs187091502	2	112577962	*ANAPC1*	t	c	0.202	0.028	3.37E-13	++	0
rs201745139	2	112578794	*ANAPC1*	t	c	-0.196	0.027	8.65E-13	--	0
rs66739581	2	112580971	*ANAPC1*	t	c	-0.192	0.027	6.14E-13	--	0
rs150954153	2	112581910	*ANAPC1*	a	g	-0.195	0.027	1.09E-12	--	0
rs12614297	2	112583476	*ANAPC1*	t	c	0.195	0.027	9.38E-13	++	0
rs56307072	2	112584242	*ANAPC1*	a	t	-0.177	0.027	8.59E-11	--	0
rs11122983	2	112584291	*ANAPC1*	a	g	0.196	0.027	7.56E-13	++	0
rs7580454	2	112587099	*ANAPC1*	t	c	0.184	0.025	6.31E-13	++	0

rs11675449	2	112589080	*ANAPC1*	a	g	0.194	0.027	1.14E-12	++	0
rs11674974	2	112591840	*ANAPC1*	a	g	-0.194	0.027	1.20E-12	--	0
rs35212506	2	112594570	*ANAPC1*	c	g	-0.194	0.027	1.48E-12	--	0
rs11683345	2	112597057	*ANAPC1*	t	c	0.194	0.027	1.36E-12	++	0
rs12617909	2	112598119	*ANAPC1*	t	c	0.193	0.027	1.72E-12	++	0
rs12992603	2	112598534	*ANAPC1*	c	g	-0.191	0.027	1.22E-12	--	0
rs11122990	2	112599436	*ANAPC1*	t	c	0.194	0.027	1.17E-12	++	0
rs11674795	2	112602249	*ANAPC1*	a	t	-0.192	0.027	1.96E-12	--	0
rs10779879	2	112603408	*ANAPC1*	t	c	0.193	0.027	1.52E-12	++	0
rs74182847	2	112604183	*ANAPC1*	a	g	-0.193	0.027	1.68E-12	--	0
rs71413401	2	112604685	*ANAPC1*	t	c	-0.193	0.027	1.63E-12	--	0
rs74189873	2	112606330	*ANAPC1*	a	g	0.194	0.027	1.24E-12	++	0
rs3877249	2	112615253	*ANAPC1*	t	c	0.194	0.027	1.42E-12	++	0
rs76292584	2	112619067	*ANAPC1*	a	g	0.193	0.027	1.46E-12	++	0
rs11689168	2	112621199	*ANAPC1*	t	c	-0.193	0.027	1.55E-12	--	0
rs34432308	2	112626193	*ANAPC1*	t	c	0.191	0.027	2.33E-12	++	0
rs35366113	2	112629488	*ANAPC1*	a	t	0.191	0.027	2.55E-12	++	0
rs80233695	2	112633047	*ANAPC1*	t	c	-0.192	0.027	1.82E-12	--	0
rs113894504	2	112633092	*ANAPC1*	c	g	-0.191	0.027	2.50E-12	--	0
rs1548189	2	112633562	*ANAPC1*	t	g	0.186	0.027	3.37E-12	++	0
rs13000524	2	112637867	*ANAPC1*	t	g	-0.193	0.027	1.56E-12	--	0
rs71414609	2	112640229	*ANAPC1*	a	g	0.185	0.027	4.50E-12	++	0
rs35533505	2	112640543	*ANAPC1*	c	g	0.185	0.027	4.87E-12	++	0
rs17835589	2	112641149	*ANAPC1*	c	g	0.182	0.026	5.05E-12	++	0
rs71414610	2	112641266	*ANAPC1*	c	g	0.185	0.027	4.34E-12	++	0
rs56009602	11	130419717	*ADAMTS8*	t	c	0.344	0.059	4.29E-09	++	0
rs2721043	13	41078668	*FOXO1*	a	c	-0.216	0.039	3.62E-08	--	0
rs2755238	13	41110270	*FOXO1*	t	c	0.245	0.037	6.33E-11	++	0

rs2721051	13	41110884	*FOXO1*	t	c	-0.246	0.037	4.48E-11	--	0
rs74948688	13	41110922	*FOXO1*	t	c	-0.264	0.046	1.11E-08	--	0
rs79728429	13	41114572	*FOXO1*	t	c	-0.281	0.048	4.75E-09	--	0
rs2701857	13	41115586	*FOXO1*	a	c	0.246	0.038	5.63E-11	++	0
rs11616662	13	41119466	*FOXO1*	a	g	-0.245	0.038	6.69E-11	--	0
rs28378192	16	88329659	*ZNF469*	t	c	0.137	0.025	2.52E-08	++	0
rs12448211	16	88330512	*ZNF469*	a	g	0.138	0.025	1.73E-08	++	0
rs77542162	17	67081278	*ABCA6*	a	g	-0.538	0.082	6.56E-11	--	71

eTable 4. Genome-wide Significant SNPs From Meta-analysis of Corneal Resistance Factor GWAS in EPIC-Norfolk and TwinsUK

Alternate shading is used to highlight different loci, and the nearest gene at each locus is presented.

rs ID	Chromosome	Position	Nearest gene to locus	Allele1	Allele2	Beta	Standard error	*P*-value	Direction	I-squared
rs78658973	2	112484525	*ANAPC1*	a	t	0.202	0.031	3.8E-11	++	0
rs142498660	2	112484861	*ANAPC1*	t	c	0.203	0.031	3.7E-11	++	0
rs114204453	2	112486894	*ANAPC1*	a	g	0.201	0.031	5.7E-11	++	0
rs12612620	2	112488876	*ANAPC1*	a	g	0.202	0.031	4.0E-11	++	0
rs371809230	2	112489416	*ANAPC1*	a	g	0.202	0.031	4.1E-11	++	0
rs201205018	2	112490128	*ANAPC1*	a	g	0.201	0.031	5.5E-11	++	0
rs72823439	2	112490328	*ANAPC1*	t	g	-0.200	0.031	7.3E-11	--	0
rs77403931	2	112490371	*ANAPC1*	c	g	-0.204	0.031	2.8E-11	--	0
rs72823440	2	112490418	*ANAPC1*	a	g	0.202	0.031	4.3E-11	++	0
rs71252597	2	112492986	*ANAPC1*	t	c	-0.211	0.032	5.6E-11	--	0
rs143231698	2	112493732	*ANAPC1*	a	g	-0.210	0.032	6.5E-11	--	0
rs145274367	2	112494600	*ANAPC1*	a	c	0.201	0.031	4.8E-11	++	0
rs149542794	2	112496121	*ANAPC1*	a	t	0.200	0.030	4.9E-11	++	0
rs200632716	2	112496958	*ANAPC1*	a	c	0.199	0.030	5.4E-11	++	0
rs74267315	2	112498114	*ANAPC1*	a	g	-0.201	0.030	4.1E-11	--	0
rs17040773	2	112500035	*ANAPC1*	a	c	-0.199	0.030	3.3E-11	--	0
rs71226248	2	112506511	*ANAPC1*	t	c	0.199	0.030	3.1E-11	++	0
rs150306256	2	112506733	*ANAPC1*	t	c	-0.199	0.030	3.5E-11	--	0
2:112520793	2	112520793	*ANAPC1*	a	g	-0.200	0.030	1.4E-11	--	0
rs114755846	2	112520920	*ANAPC1*	a	t	-0.199	0.030	1.9E-11	--	0
rs2948006	2	112521945	*ANAPC1*	a	g	0.197	0.030	3.8E-11	++	0
rs137999262	2	112526866	*ANAPC1*	a	g	0.199	0.030	2.8E-11	++	0
rs147346361	2	112529050	*ANAPC1*	a	g	-0.199	0.030	2.6E-11	--	0

rs79671094	2	112531691	*ANAPC1*	a	g	0.200	0.030	3.5E-11	++	0
rs76210128	2	112532987	*ANAPC1*	t	c	0.199	0.030	2.9E-11	++	0
rs200193771	2	112538247	*ANAPC1*	a	g	0.190	0.029	9.3E-11	++	0
rs77797441	2	112539384	*ANAPC1*	t	c	0.209	0.031	8.0E-12	++	0
rs78676279	2	112543377	*ANAPC1*	t	c	0.190	0.029	9.1E-11	++	0
rs80125903	2	112549693	*ANAPC1*	a	c	0.190	0.029	9.7E-11	++	0
rs202110867	2	112550325	*ANAPC1*	c	g	-0.204	0.030	1.0E-11	--	0
rs189319935	2	112550621	*ANAPC1*	a	g	-0.204	0.031	5.2E-11	--	0
rs190739040	2	112552427	*ANAPC1*	t	c	0.197	0.030	4.6E-11	++	0
rs192541479	2	112552967	*ANAPC1*	a	t	-0.198	0.030	4.5E-11	--	0
rs200623464	2	112554527	*ANAPC1*	t	g	0.198	0.030	3.6E-11	++	0
rs141660957	2	112554577	*ANAPC1*	t	c	0.198	0.030	3.2E-11	++	0
rs200015423	2	112558479	*ANAPC1*	a	g	-0.199	0.030	2.6E-11	--	0
rs201175214	2	112559582	*ANAPC1*	a	g	-0.191	0.029	7.3E-11	--	0
rs142711068	2	112560090	*ANAPC1*	a	g	0.191	0.029	8.9E-11	++	0
rs202074374	2	112564426	*ANAPC1*	a	c	-0.190	0.029	1.0E-10	--	0
rs201128688	2	112566517	*ANAPC1*	t	c	0.187	0.029	1.9E-10	++	0
rs201709611	2	112567624	*ANAPC1*	c	g	-0.186	0.029	2.0E-10	--	0
rs113870763	2	112567980	*ANAPC1*	t	c	-0.187	0.029	2.0E-10	--	0
rs187091502	2	112577962	*ANAPC1*	t	c	0.200	0.030	3.7E-11	++	0
rs201745139	2	112578794	*ANAPC1*	t	c	-0.193	0.030	1.0E-10	--	0
rs66739581	2	112580971	*ANAPC1*	t	c	-0.189	0.029	9.4E-11	--	0
rs150954153	2	112581910	*ANAPC1*	a	g	-0.192	0.030	1.3E-10	--	0
rs12614297	2	112583476	*ANAPC1*	t	c	0.192	0.030	1.2E-10	++	0
rs56307072	2	112584242	*ANAPC1*	a	t	-0.197	0.030	3.3E-11	--	0
rs11122983	2	112584291	*ANAPC1*	a	g	0.193	0.030	8.9E-11	++	0
rs7580454	2	112587099	*ANAPC1*	t	c	0.189	0.028	1.1E-11	++	0
rs11675449	2	112589080	*ANAPC1*	a	g	0.192	0.030	1.3E-10	++	0

rs11674974	2	112591840	*ANAPC1*	a	g	-0.191	0.030	1.3E-10	--	0
rs35212506	2	112594570	*ANAPC1*	c	g	-0.191	0.030	1.7E-10	--	0
rs11683345	2	112597057	*ANAPC1*	t	c	0.191	0.030	1.5E-10	++	0
rs12617909	2	112598119	*ANAPC1*	t	c	0.190	0.030	1.8E-10	++	0
rs12992603	2	112598534	*ANAPC1*	c	g	-0.187	0.029	1.8E-10	--	0
rs11122990	2	112599436	*ANAPC1*	t	c	0.192	0.030	1.3E-10	++	0
rs11674795	2	112602249	*ANAPC1*	a	t	-0.191	0.030	1.6E-10	--	0
rs10779879	2	112603408	*ANAPC1*	t	c	0.191	0.030	1.5E-10	++	0
rs74182847	2	112604183	*ANAPC1*	a	g	-0.191	0.030	1.5E-10	--	0
rs71413401	2	112604685	*ANAPC1*	t	c	-0.190	0.030	1.8E-10	--	0
rs74189873	2	112606330	*ANAPC1*	a	g	0.192	0.030	1.2E-10	++	0
rs3877249	2	112615253	*ANAPC1*	t	c	0.192	0.030	1.2E-10	++	0
rs76292584	2	112619067	*ANAPC1*	a	g	0.191	0.030	1.3E-10	++	0
rs11689168	2	112621199	*ANAPC1*	t	c	-0.191	0.030	1.3E-10	--	0
rs34432308	2	112626193	*ANAPC1*	t	c	0.189	0.030	2.2E-10	++	0
rs35366113	2	112629488	*ANAPC1*	a	t	0.189	0.030	2.2E-10	++	0
rs80233695	2	112633047	*ANAPC1*	t	c	-0.190	0.030	1.4E-10	--	0
rs113894504	2	112633092	*ANAPC1*	c	g	-0.189	0.030	2.3E-10	--	0
rs1548189	2	112633562	*ANAPC1*	t	g	0.183	0.029	3.5E-10	++	0
rs13000524	2	112637867	*ANAPC1*	t	g	-0.191	0.030	1.4E-10	--	0
rs71414609	2	112640229	*ANAPC1*	a	g	0.178	0.029	1.0E-09	++	0
rs35533505	2	112640543	*ANAPC1*	c	g	0.177	0.029	1.2E-09	++	0
rs17835589	2	112641149	*ANAPC1*	c	g	0.174	0.029	1.5E-09	++	0
rs71414610	2	112641266	*ANAPC1*	c	g	0.178	0.029	1.1E-09	++	0
rs6445054	3	172274219	*FNDC3B*	t	c	0.194	0.034	1.38E-08	++	0
rs6445055	3	172274597	*FNDC3B*	a	g	-0.193	0.034	1.68E-08	--	0
rs6800129	3	172278729	*FNDC3B*	c	g	0.191	0.034	1.86E-08	++	0
rs4894414	3	172279709	*FNDC3B*	t	c	-0.191	0.034	2.08E-08	--	0

rs56009602	11	130419717	*ADAMTS8*	t	c	0.376	0.064	3.34E-09	++	0
rs2721043	13	41078668	*FOXO1*	a	c	-0.235	0.043	4.3E-08	--	0
rs2755238	13	41110270	*FOXO1*	t	c	0.267	0.041	6.2E-11	++	0
rs2721051	13	41110884	*FOXO1*	t	c	-0.268	0.041	5.2E-11	--	0
rs74948688	13	41110922	*FOXO1*	t	c	-0.302	0.050	2.0E-09	--	0
rs79728429	13	41114572	*FOXO1*	t	c	-0.306	0.052	4.8E-09	--	0
rs2701857	13	41115586	*FOXO1*	a	c	0.266	0.041	8.6E-11	++	0
rs11616662	13	41119466	*FOXO1*	a	g	-0.265	0.041	1.1E-10	--	0
rs72755233	15	100152748	*ADAMTS17*	a	g	0.233	0.043	4.48E-08	++	0
rs7185012	16	88293631	*ZNF469*	a	t	0.159	0.028	1.3E-08	++	0
rs12447690	16	88298124	*ZNF469*	t	c	0.160	0.026	1.1E-09	++	0
rs7201034	16	88298705	*ZNF469*	a	g	-0.166	0.027	5.9E-10	--	0
rs7500824	16	88299491	*ZNF469*	a	g	-0.161	0.026	1.2E-09	--	0
rs35542380	16	88299593	*ZNF469*	c	g	0.162	0.027	1.3E-09	++	0
rs7498219	16	88300110	*ZNF469*	t	c	0.157	0.026	2.6E-09	++	0
rs6540214	16	88301976	*ZNF469*	a	g	0.161	0.027	1.9E-09	++	0
rs7405095	16	88307825	*ZNF469*	a	g	-0.163	0.027	1.8E-09	--	0
rs6540217	16	88310910	*ZNF469*	a	g	-0.167	0.027	7.8E-10	--	0
rs200073183	16	88311533	*ZNF469*	t	c	-0.160	0.027	6.4E-09	--	0
rs12919641	16	88312600	*ZNF469*	c	g	0.171	0.027	5.0E-10	++	0
rs12925350	16	88312692	*ZNF469*	t	c	-0.167	0.027	7.8E-10	--	0
rs71372762	16	88313227	*ZNF469*	t	c	0.157	0.027	7.6E-09	++	0
rs62047083	16	88313255	*ZNF469*	a	g	-0.159	0.027	4.1E-09	--	0
rs8059024	16	88314163	*ZNF469*	t	c	-0.161	0.027	2.3E-09	--	0
rs11117401	16	88314452	*ZNF469*	a	g	0.163	0.027	1.3E-09	++	0
rs6540220	16	88315515	*ZNF469*	c	g	0.160	0.027	2.7E-09	++	0
rs7198116	16	88318648	*ZNF469*	t	c	-0.160	0.027	2.6E-09	--	0
rs12711488	16	88319421	*ZNF469*	c	g	-0.159	0.027	3.3E-09	--	0

rs7498700	16	88320620	*ZNF469*	t	c	-0.161	0.027	2.0E-09	--	0
rs7501109	16	88320862	*ZNF469*	c	g	0.163	0.027	1.3E-09	++	0
rs7501402	16	88320911	*ZNF469*	a	t	-0.163	0.027	1.2E-09	--	0
rs7403826	16	88321167	*ZNF469*	a	t	-0.163	0.027	1.2E-09	--	0
rs6540223	16	88321436	*ZNF469*	t	c	0.160	0.027	2.5E-09	++	0
rs58577366	16	88323323	*ZNF469*	t	c	0.169	0.027	3.8E-10	++	0
rs28425635	16	88323599	*ZNF469*	a	g	0.173	0.027	1.3E-10	++	0
rs58657775	16	88323829	*ZNF469*	a	g	0.165	0.027	8.3E-10	++	0
rs28493272	16	88324245	*ZNF469*	t	c	-0.171	0.027	1.9E-10	--	0
rs28715745	16	88324562	*ZNF469*	a	g	0.168	0.027	4.1E-10	++	0
rs28716598	16	88324563	*ZNF469*	c	g	-0.169	0.027	3.3E-10	--	0
rs35479534	16	88324754	*ZNF469*	a	g	0.173	0.027	1.3E-10	++	0
rs35193497	16	88324821	*ZNF469*	t	g	-0.176	0.027	6.2E-11	--	0
rs28698209	16	88324931	*ZNF469*	t	g	-0.174	0.027	9.1E-11	--	0
rs28411862	16	88325560	*ZNF469*	c	g	-0.174	0.027	1.1E-10	--	0
rs28481824	16	88326166	*ZNF469*	t	c	-0.166	0.027	7.4E-10	--	0
rs34715091	16	88326782	*ZNF469*	a	g	0.170	0.027	1.4E-10	++	0
rs28445880	16	88327422	*ZNF469*	t	g	-0.167	0.027	2.9E-10	--	0
rs28563118	16	88327569	*ZNF469*	c	g	0.169	0.027	1.8E-10	++	0
rs28687756	16	88328928	*ZNF469*	t	g	-0.178	0.027	4.1E-11	--	0
rs28526212	16	88329202	*ZNF469*	a	g	0.170	0.026	1.2E-10	++	0
rs28378192	16	88329660	*ZNF469*	t	c	0.170	0.026	5.5E-11	++	0
rs12719932	16	88330349	*ZNF469*	a	g	-0.171	0.026	5.0E-11	--	0
rs12448211	16	88330513	*ZNF469*	a	g	0.170	0.026	5.1E-11	++	0
rs12926024	16	88331309	*ZNF469*	t	c	-0.158	0.026	7.6E-10	--	0
rs9934580	16	88331515	*ZNF469*	a	g	-0.157	0.026	1.0E-09	--	0
rs9938149	16	88331640	*ZNF469*	a	c	0.156	0.026	1.1E-09	++	0
rs8059298	16	88332479	*ZNF469*	t	c	-0.161	0.026	3.9E-10	--	0

rs11259972	16	88333296	*ZNF469*	t	c	-0.162	0.026	3.6E-10	--	0
rs9922572	16	88334112	*ZNF469*	a	c	-0.170	0.027	2.9E-10	--	0
rs9926214	16	88334441	*ZNF469*	t	c	0.161	0.026	7.7E-10	++	0
rs12719930	16	88335774	*ZNF469*	a	g	0.162	0.026	7.8E-10	++	0
rs12719931	16	88335776	*ZNF469*	t	c	0.162	0.026	7.4E-10	++	0
rs8057716	16	88335790	*ZNF469*	c	g	0.157	0.027	3.8E-09	++	0
rs12935558	16	88336978	*ZNF469*	a	g	0.157	0.026	1.8E-09	++	0
rs12935576	16	88337013	*ZNF469*	a	g	0.155	0.026	2.4E-09	++	0
rs12918094	16	88337319	*ZNF469*	a	g	-0.155	0.026	2.4E-09	--	0
rs9925231	16	88338107	*ZNF469*	t	c	-0.153	0.026	4.5E-09	--	0
rs7404292	16	88338467	*ZNF469*	a	g	-0.156	0.027	5.1E-09	--	0
rs6603048	16	88340921	*ZNF469*	t	c	-0.157	0.027	5.9E-09	--	0
rs7199889	16	88342639	*ZNF469*	c	g	-0.156	0.026	3.8E-09	--	0
rs9938961	16	88343597	*ZNF469*	a	g	-0.158	0.029	4.2E-08	--	0
rs149540885	18	52877255	*TCF4*	t	c	0.441	0.080	3.3E-08	++	63
rs11659764	18	53335512	*TCF4*	a	t	-0.320	0.054	3.9E-09	--	0
rs784256	18	53398626	*TCF4*	a	g	0.178	0.032	3.5E-08	++	0
rs148766287	21	47404422	*COL6A1*	c	g	0.705	0.109	8.7E-11	++	0
rs142493024	21	47413793	*COL6A1*	a	g	-0.719	0.108	2.9E-11	--	0
rs182804464	21	47420667	*COL6A1*	c	g	0.731	0.107	1.0E-11	++	0

eTable 5. Corneal Tissue Specific Expression Profiles

Publicly available corneal RNA-seq data were analysed to determine the expression profile of selected genes from 2 distinct data sets. Data were retrieved from three human adult and two human fetal corneal endothelial samples (Chen et al., 2013) and from four distinct human limbal compartments; the basal limbal crypts (BLCs), the superficial limbal crypts (SLCs), the paracentral/central corneal epithelium (CE), and the adjacent limbal stroma (LS) (Bath et al., 2013). Data are presented as TPM (transcripts per million).

	Expression (TPM)								
	Corneal Endothelium					Limbal Compartments			
	Adult			Fetal		BLCs	CE	LS	SLCs
Gene	1	2	3	1	2				
ANAPC1	11.12	7.43	12.27	14.54	10.46	11.08	10.34	3.85	8.92
ADAMTS8	0.06	0.00	0.06	3.56	3.69	0.06	0.02	0.24	0.00
ADAMTS17	1.43	1.95	0.73	4.45	2.37	1.57	0.85	0.43	0.77
ABCA6	13.55	8.75	3.17	2.00	0.68	4.64	4.88	119.41	2.64
COL6A1	124.18	113.61	113.23	1041.27	957.61	2.78	1.31	62.82	1.49

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